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Effect of red cell distribution width (RDW) on short-term mortality and morbidity in patients with acute coronary syndrome

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Abstract

Aim: Previous studies in the literature have shown that high RDW values are significantly associated with coronary artery disease (CAD), heart failure, and peripheral artery disease. The prognostic value of RDW for CAD in the preliminary period was discussed in the limited literature. In this study, it was aimed to investigate the relationship between red cell distribution width (RDW) and the mortality and morbidity of acute coronary syndrome (ACS) in a 1-year follow-up.
Material and Methods: This study had a retrospective design. It enrolled patients who had their first ACS. Age, sex distribution and the levels of RDW, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were determined. Mortality rates by the first month and the first year were determined. The 1-year rates of recurrent ACS, percutaneous coronary intervention (PCI), and heart failure were also recorded.
Results: The data of 132 patients were analyzed. The survival rate was 85.6% (n=113) at 1 month and 74.2% (n=98) at 1 year. RDW was significantly lower in patients who survived at 1 month and 1 year ($p<0.001$ and $p=0.004$, respectively). In the 1-year follow-up, RDW was significantly higher in patients who had ACS, who underwent PCI, and who developed heart failure ($p=0.021$, 0.001, and 0.001, respectively). A significant increase of 11.5% was found in 1-year mortality for RDW levels above 14.1% (Hazard ratio=3.24, 95% CI: 1.58-6.66; $p=0.001$).
Discussion: The RDW level is a simple, fast, and reliable parameter in deciding the prognosis of patients with ACS admitted to the emergency department.

Keywords
Red cell distribution width; RDW; Coronary artery disease; Mortality; Morbidity

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Introduction

Red cell distribution width-standard deviation (RDW-SD, fL) and red cell distribution width-variation coefficient (RDW-CV, %) are considered markers of anisocytosis and routinely reported in automatic complete blood counts to make a differential diagnosis of anemia [1,2]. RDW is positively correlated with age and hemoglobin level [3]. Previous studies in the literature have shown that high RDW values are significantly associated with coronary artery disease (CAD), heart failure, and peripheral artery disease [4,5]. Recent studies have described a relationship between RDW and mortality in acute myocardial infarction (AMI) [6,7]. Azab et al. found that patients with RDW >14% had a significantly higher 4-year mortality than patients with RDW <14%. (30% vs 7%, respectively; p<0.0001) [4]. Nagula et al. found a positive correlation between high RDW level and the AMI severity and calculated that RDW above a threshold value of 14.3% had a sensitivity of 58.9% and a specificity of 84.8% for CAD on coronary angiography (CAG) [8]. Poludasu et al. found a 4-year survival rate of 70% in patients with RDW >15.7 and 85% in patients with RDW <13.3%, with the difference being statistically significant (p<0.001) [9]. In the present study, we aimed to investigate the relationship between RDW at admission and 1-year mortality and morbidity in patients with acute coronary syndrome.

Material and Methods

This study was retrospectively designed and enrolled patients who were diagnosed with AMI in the emergency department of a secondary state hospital and referred for CAG between 2016 and 2020. The study data were obtained from patient files and archive records. The study included patients older than 18 years of age with objective evidence of AMI, whose 1-year medical records after the initial diagnosis were available. Patients with a previous history of AMI, PAG, coronary artery bypass surgery, end-stage renal disease, cancer, thalassemia, or bleeding diathesis were excluded. Patients with age older than 85 years, clinical evidence of active infection, active or chronic inflammatory or autoimmune disease, steroid use, and anemia were also excluded. Age, gender distribution, admission RDW, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) levels were determined. The rates of survival and recurrent ACS, CAG intervention, and heart failure at 1 month and 1 year were also recorded. The patients were divided into two groups below and above the median values of RDW, HDL, and LDL levels.

Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as percentages. Student's t-test or analysis of variance was used to compare parametric continuous variables; Mann-Whitney U-test or Kruskal-Wallis test was used to compare nonparametric continuous variables. The x^2 test was used to compare categorical variables. ROC analysis was used to determine a clinical threshold value for RDW values. Multivariate logistic regression analysis was used to determined variables associated with mortality. Survival analysis was performed using Kaplan-Meier curves. SPSS 22.0 program (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. This study was performed in compliance with the 1964 Helsinki Declaration and its subsequent amendments. Ethics committee approval for the study was obtained from the affiliated institution (No:459; Date:15.08.2020).

Results

Medical records of 239 patients were reviewed and data of 132 patients meeting the inclusion criteria were included in the final analysis. The mean age of the patients was 66.4±10.2 years. The number of females was 60 (45.5%) and the number of males was 72 (54.5%). ACS occurred in the form of STEMI in 24 (18.2%) patients and NON-STEMI in 108 (81.8%) patients. The survival rate was 85.6% (n=113) at 1 month and 74.2% (n=98) at 1 year. The study findings are summarized in Table 1 and Table 2.

Table 1. Summary of the categoric variables

	n	%
Sex		
Female	60	45.5
Male	72	54.5
ACS		
STEMI	24	18.2
NONSTEMI	108	81.8
1-year survival status		
Deceased	34	25.8
Survived	98	74.2
ACS at 1 year		
ACS (-)	102	77.3
Recurrent ACS	30	22.7
CAG at 1 year		
KAG (-)	123	93.2
KAG (+)	9	6.8
Age (median)		
<66	64	48.5
≥66	68	51.5
RDWSD (median)		
<55	96	72.7
≥55	36	27.3
RDWCV (median)		
<14.1	74	56.1
≥14.1	58	43.9
HDL (median)		
<43	79	59.8
≥43	53	40.2
LDL (median)		
<143	68	51.5
≥143	64	48.5

Table 2. Summary of the continuous variables

	Mean	SD	Min	Max
Age	66.47	10.27	44.00	84.00
RDWSD	55.12	12.30	43.30	78.60
RDWCV	14.11	1.16	12.70	16.30
HDL	43.55	7.00	33.00	61.00
LDL	143.60	30.16	110.00	295.00

Table 3. Relationship of the study parameters with mortality and morbidity, and t-test statistics

	Survival status at 1 year					ACS at 1 year					CAG at 1 year				
	Deceased		Survived		p	ACS (-)		ACS (+)		p	CAG (-)		CAG (+)		p
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Age	63.4	11.3	67.5	9.7	0.046	65.7	10.7	69.2	8.1	0.102	66.3	10.5	69.1	7.0	0.426
RDWSD	59.7	12.8	53.5	11.8	0.012	54.4	12.0	57.6	13.2	0.203	54.2	11.7	67.0	14.9	0.002
RDWCV	14.6	.9	13.9	1.2	0.001	14.0	1.1	14.5	1.1	0.021	14.0	1.1	15.4	.7	0.001
HDL	39.5	6.3	44.9	6.7	0.001	43.7	6.9	43.1	7.4	0.710	43.4	7.1	45.8	4.5	0.325
LDL	161.4	30	137.4	27.8	0.001	146.2	31.5	134.7	23.5	0.066	144.2	30.9	135.2	17.0	0.390

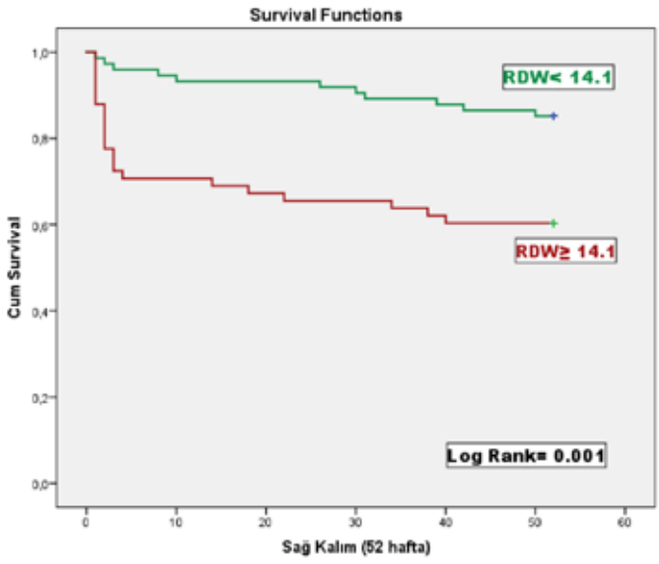

Figure 1. Kaplan-Meier curves of 1-year survival according to the median RDW value

The RDW was 14.9±0.6% in patients who died and 13.9±1.1% in those who survived by 1 month (p <0.001; 95% CI: 0.6-1.3). The RDW was 13.9±1.1% in survivors at 1 year and 14.6±0.8% in patients who died from ACS, with the difference being statistically significant (p= 0.004; 95% CI:0.2-1.0). The RDW was 15.2±0.6% in patients who developed heart failure by 1 year after ACS and 14.0±1.1% in those who did not develop heart failure, with the difference being statistically significant (p=0.00; 95% CI:0.3-2.0). The relationship of other parameters with mortality and morbidity, and the t-test statistics are shown in Table 3.

In our study, the median value of RDW was 14.1%. According to the Kaplan-Meier survival analysis, 1-year survival was statistically higher in patients with RDW ≥14.1% (Log-rank test p=0.001, Figure 1). Strikingly, the mortality rate was 9 times higher in patients with RDW above the median value of 14.1% by 1 month after ACS (Odds ratio (OR)=9.09, 95% CI: 2.4-33.2, p<0.001). According to the Cox regression analysis, a significant increase of 11.5% was found in 1-year mortality for higher RDW levels (Hazard ratio: HR=3.24, 95% CI: 1.58-6.66; p = 0.001).

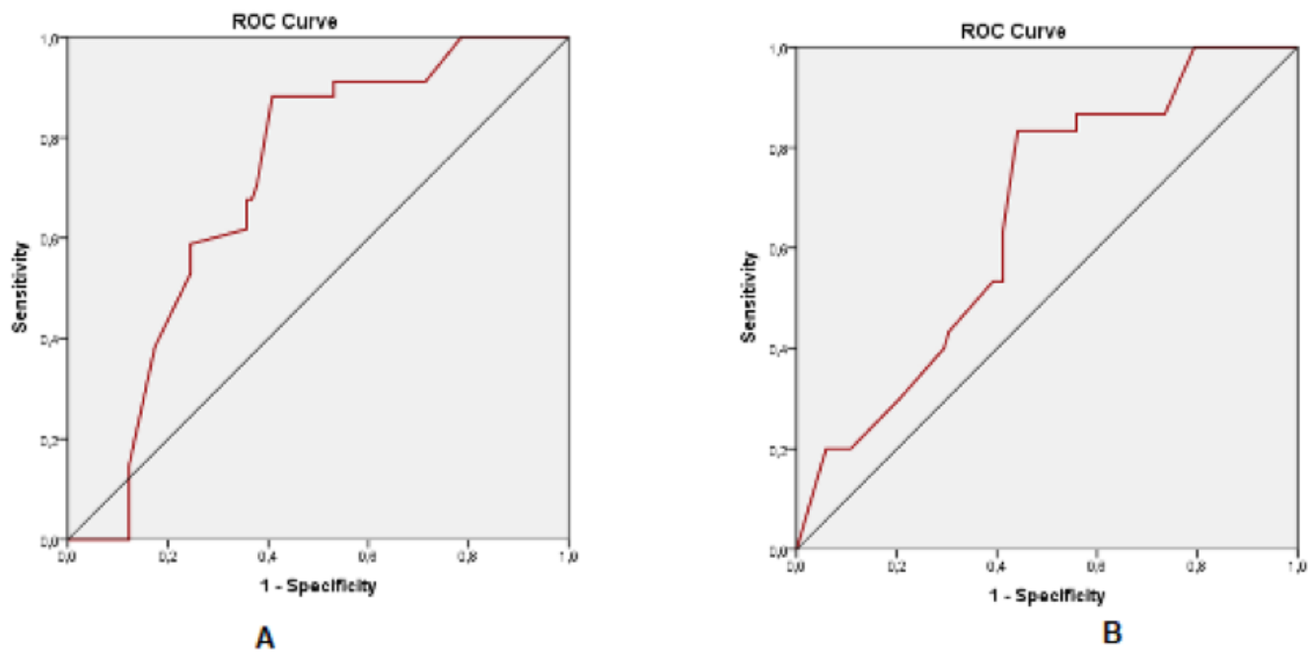

Figure 2. ROC curve of parameters
A: ROC curve of RDW for survival prediction at 1 year (AUC: 0.710)
B: ROC curve of RDW for the prediction of recurrent ACS at 1 year (AUC: 0.662)

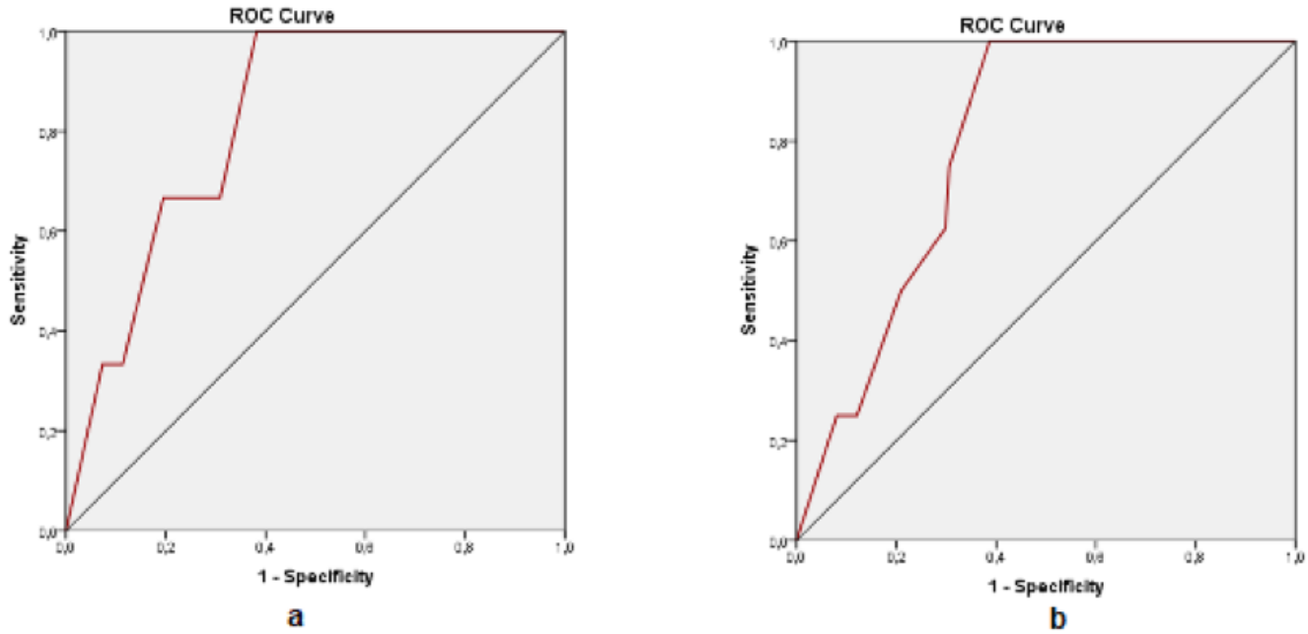

Figure 3. ROC curve of Parameters
a: ROC curve of RDW for the prediction of CAG at 1 year (AUC: 0.821)
b: ROC curve of RDW for the prediction of new-onset heart failure at 1 year (AUC: 0.792)

According to the ROC analysis, the cut-off value of 14.2% for RDW had a sensitivity of 67.6% and a specificity of 64.3% for 1-year mortality following ACS (AUC: 0.710, 95% CI: 0.620-0.800, Figure 2A). The cut-off value of 13.9% for RDW had a sensitivity of 56.7% and a specificity of 58.8% for recurrent ACS by 1 year (AUC: 0.662, 95% CI: 0.560-0.163, Figure 2B). The cut-off value of 14.7% for RDW had a sensitivity of 66.7% and a specificity of 69.1% for undergoing CAG by 1 year (AUC: 0.821, 95% CI: 0.723-0.919, Figure 3a). The cut-off value of 14.7% for RDW had a sensitivity of 75.1% and a specificity of 69.4% for the development of heart failure (AUC: 0.792, 95% CI: 0.692-0.892, Figure 3b).

Discussion

This study showed a relationship between high RDW values and ACS-related mortality, recurrent ACS, the development of new-onset heart failure, and CAG intervention in the early post-ACS period. Especially in the very early period after ACS, mortality was significantly higher on average by 9 times (OR) among patients with an RDW value above the median value of 14.1%.

RDW reflects variability in the size of peripheral erythrocytes and is based on the width of the volume distribution curve, with larger values showing greater variability (anisocytosis). RDW is altered by the levels of iron, B12, or folate, or hemolysis [6,10,11].

In the Tromsø Study, which started with 25,612 participants in 1994-1995, a 13% increase in the ACS risk was found for each 1% increase in RDW at the end of 15.8 years of follow-up (HR=1.13) [12]. Cemin et al. showed that RDW was a significant marker for ACS among 1971 patients admitted to the emergency department with chest pain [13]. In that study, they found that a cut-off value of 13.7% for RDW had a sensitivity of 75% and a specificity of 52% for the presence of ACS (AUC: 0.610). Felker et al. reported that a higher RDW level was a strong and independent marker of morbidity and mortality in patients with chronic heart failure [14]. Van Kimmenade et al. found a significant 1.03-fold increase in mortality risk for each 1% increase in RDW during the 1-year follow-up period in patients with acute heart failure (p=0.04) [15]. In addition, a significant relationship has been shown between high RDW level and cardiovascular death and hospitalizations due to heart failure [16-18].

In a prospective study involving 310 patients presenting with ACS, Akın et al. found high RDW level to be a significant risk factor for CAD severity (OR=1.16, p=0.021) [19]. Gül et al. found a cardiovascular mortality rate of 18% in the high RDW group and 12% in the low RDW group at a follow-up of 3 years (p<0.001) [20]. In addition, they reported a 6-month mortality rate of 9.5% in the high RDW group and 1.9% in the low RDW group (p=0.002). Similarly, the 6-month and 3-year rates for recurrent ACS were significantly higher in the high-RDW group than in the low-RDW group (27.4% versus 13.7%; p=0.03, and 10.7% versus 6%; p <0.001, respectively). Similarly, we categorized our patients into two groups as those with RDW≤ 14 and those with RDW>14. We demonstrated that the rate of hospitalization due to heart failure was 16.8% in the high-RDW group and 7.9% in the low-RDW group by 3 years (p=0.020). Furthermore, our ROC analysis found that an RDW value of 14% was a significant cut-off value for 3-year cardiovascular death (AUC: 0.70, sensitivity 60%, specificity 72.5%) [20]. Wang et al. found that the rates of mortality and heart failure among 1604 patients were significantly higher in the high-RDW group by 1 month after ACS (OR=2.1 p<0.001 and OR=2.1, p<0.001, respectively) [21]. In 2506 patients who underwent CAG for STEMI, Uyarel et al. found an in-hospital mortality rate of 7.6% in the high-RDW group (mean 16.1±1.6%) and 3.6% in the low-RDW group (mean 13.4±0.8%) (p<0.001) [22]. In that study, where the RDW median value was taken as 14.8%, the rates of cardiovascular mortality (11.4% versus 4.4%), recurrent ACS (10.2% versus 7.8%), and heart failure (11.1% versus 7%) were

significantly higher in the high-RDW group at a mean follow-up of 21 months (p <0.001, p=0.080, and p=0.003, respectively). In this study, an 83% increase in long-term mortality was found for high RDW levels, thus RDW level was an independent risk factor (HR=1.831).

In our study, an average of 9-fold mortality increase was found for high RDW levels at a follow-up of 1 month (Odds ratio (OR)=9.09, 95% CI: 2.4-33.2). Similarly, a high RDW level was found to be an independent risk factor for 1-year mortality (HR=3.24%, 95CI: 1.58-6.66). Furthermore, in accordance with the literature, a high RDW level was found to be a significant risk factor for the development of ACS, CAG intervention, and heart failure. In this study, the relative risk ratios were found to be higher compared with similar studies. This may be due to our smaller sample size. In addition, our study power may be insufficient to investigate the cause of death during the follow-up period due to its retrospective design. However, its results are consistent with the findings reported by other prospective studies.

Conclusion

High RDW level is a significant risk factor for early mortality and morbidity in ACS. The RDW level is a simple, fast, and reliable parameter in making decisions for and determining the prognosis of patients with ACS who are admitted to the emergency department.

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Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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